

We claim:

1. A peptide fragment having the general sequence

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His-X<sup>1</sup>-His-X<sup>2</sup>-X<sup>3</sup>-X<sup>4</sup>-Cys-X<sup>5</sup>-X<sup>6</sup>-Cys,

where the variables X<sup>1</sup> to X<sup>6</sup> in the sequence have the following meanings:

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X<sup>1</sup> = an amino acid selected from the group of Ala, Val, Phe, Ser, Met, Trp, Tyr, Asn, Asp or Lys and the variables X<sup>2</sup> to X<sup>6</sup> an amino acid selected from the group of Gly, Ala, Val, Leu, Ile, Phe, Pro, Ser, Thr, Cys, Met, Trp, Tyr, Asn, Gln, Asp, Glu, Lys, Arg, His or

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X<sup>2</sup> = an amino acid selected from the group of Val, Ile, Phe, Pro, Trp, Tyr, Gln, Glu or Arg and the variables X<sup>1</sup>, X<sup>3</sup> to X<sup>6</sup> an amino acid selected from the group of Gly, Ala, Val, Leu, Ile, Phe, Pro, Ser, Thr, Cys, Met, Trp, Tyr, Asn, Gln, Asp, Glu, Lys, Arg, His or

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X<sup>3</sup> = an amino acid selected from the group of Gly, Ile, Thr, Met, Trp, Tyr, Asn, Gln, Asp, Glu, Lys, Arg, His and the variables X<sup>1</sup>, X<sup>2</sup>, X<sup>4</sup> to X<sup>6</sup> an amino acid selected from the group of Gly, Ala, Val, Leu, Ile, Phe, Pro, Ser, Thr, Cys, Met, Trp, Tyr, Asn, Gln, Asp, Glu, Lys, Arg, His or

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X<sup>4</sup> = an amino acid selected from the group of Val, Phe, Pro, Cys, Met, Trp, Asn, Glu, Arg or His and the variables X<sup>1</sup> to X<sup>3</sup>, X<sup>5</sup>, X<sup>6</sup> an amino acid selected from the group of Gly, Ala, Val, Leu, Ile, Phe, Pro, Ser, Thr, Cys, Met, Trp, Tyr, Asn, Gln, Asp, Glu, Lys, Arg, His or

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X<sup>5</sup> = an amino acid selected from the group of Gly, Ser, Cys, Met, Trp, Asn, Glu, Lys or Arg and the variables X<sup>1</sup> to X<sup>4</sup>, X<sup>6</sup> an amino acid selected from the group of Gly, Ala, Val, Leu, Ile, Phe, Pro, Ser, Thr, Cys, Met, Trp, Tyr, Asn, Gln, Asp, Glu, Lys, Arg, His or

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X<sup>6</sup> = an amino acid selected from the group of Phe, Pro, Ser, Cys, Trp, Tyr or Gln and the variables X<sup>1</sup> to X<sup>5</sup> an amino acid selected from the group of Gly, Ala, Val, Leu, Ile, Phe, Pro, Ser, Thr, Cys, Met, Trp, Tyr, Asn, Gln, Asp, Glu, Lys, Arg, His and

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where at least one of the variables  $X^1$  to  $X^6$  in the sequence is, independently of one another, Gln or Asn.

2. A peptide fragment as claimed in claim 1, in which the  
5 variables  $X^1$  to  $X^6$  have the meanings stated in claim 1, where at least one of the variables  $X^1$  to  $X^6$  in the sequence is, independently of one another, Lys or Arg.

3. A peptide fragment as claimed in claim 1 ~~or 2~~, in which the  
10 variables  $X^1$  to  $X^6$  in the sequence have the following meanings independently of one another:

$X^1$  = an amino acid selected from the group of Ala, Val, Phe,  
15 Ser, Met, Trp, Tyr, Asn, Asp or Lys;

$X^2$  = an amino acid selected from the group of Val, Ile, Phe,  
Pro, Trp, Tyr, Gln, Glu or Arg;

$X^3$  = an amino acid selected from the group of Gly, Ile, Thr,  
20 Met, Trp, Tyr, Asn, Gln, Asp, Glu, Lys, Arg or His;

$X^4$  = an amino acid selected from the group of Val, Phe, Pro,  
Cys, Met, Trp, Asn, Glu, Arg or His;

$X^5$  = an amino acid selected from the group of Gly, Ser, Cys,  
25 Met, Trp, Asn, Glu, Lys or Arg;

$X^6$  = an amino acid selected from the group of Phe, Pro, Ser,  
30 Cys, Trp, Tyr or Gln.

4. A peptide fragment as claimed in ~~any of claims 1 to 3~~ <sup>claim 1</sup>, in  
which the variables  $X^1$  to  $X^6$  in the sequence have the  
following meanings independently of one another:

35  $X^1$  = an amino acid selected from the group of Phe, Ser, Asn,  
Asp or Lys;

$X^2$  = an amino acid selected from the group of Val, Ile, Phe,  
40 Pro, Gln, Glu or Arg;

$X^3$  = an amino acid selected from the group of Gly, Ile, Thr,  
Met, Trp, Tyr, Asn, Asp, Glu, Arg or His;

45  $X^4$  = an amino acid selected from the group of Val, Phe, Cys,  
Met, Trp, Asn, Arg or His;

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X<sup>5</sup> = an amino acid selected from the group of Gly, Ser, Cys, Met, Asn, Glu, Lys or Arg;

X<sup>6</sup> = an amino acid selected from the group of Phe, Ser, Cys, or Tyr.

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11. A peptide fragment as claimed in ~~any of claims 1 to 4~~, in which the variables X<sup>1</sup> to X<sup>6</sup> in the sequence have the following meanings independently of one another:
- X<sup>1</sup> = Asn;
- X<sup>2</sup> = Gln, Glu or Arg;
- X<sup>3</sup> = Gly, Thr or Tyr;
- X<sup>4</sup> = Asn or Arg;
- X<sup>5</sup> = Gly or Lys;
- X<sup>6</sup> = Cys.
6. A peptide fragment having the sequence
- His-Gln-His-Glu-Gly-Arg-Cys-Lys-Glu-Cys
- His-Asn-His-Arg-Tyr-Gly-Cys-Gly-Cys-Cys
- His-Arg-His-Gly-Thr-Asn-Cys-Leu-Lys-Cys
- His-Ile-His-Gln-Ser-Asn-Cys-Gln-Val-Cys.
7. A fusion protein comprising a protein fragment as claimed in ~~any of claims 1 to 6~~.
8. A nucleic acid fragment coding for a protein fragment as claimed in ~~any of claims 1 to 6~~.
9. A nucleic acid comprising a nucleic acid fragment as claimed in claim 8.
10. A nucleic acid coding for a fusion protein as claimed in claim 7.
11. A vector comprising a nucleic acid fragment as claimed in claim 8 or 10.

12. A process for preparing fusion proteins as claimed in claim 7, which comprises fusing a nucleic acid fragment ~~as claimed in claim 8~~ to a gene which codes for a protein.
- 5 13. A process for purifying fusion proteins as claimed in claim 7, which comprises
- 10 a) bringing liquids which contain the fusion protein into contact with immobilized metal ions in such a way that an affinity linkage can form between the metal ions and the fusion protein,
- b) removing unbound substances present in the liquid,
- 15 c) eluting the bound fusion protein in which [sic] the affinity linkage is abolished by changing the liquid medium and
- 20 d) collecting the purified fusion protein.
14. The use of a protein fragment as claimed in *claim 1* ~~any of claims 1 to 6~~ or of a nucleic acid fragment ~~as claimed in claim 8~~ for purifying proteins.
- 25 15. A process for preparing protein fragments able to enter into a reversible affinity linkage with immobilized metal ions, which comprises carrying out the following steps:
- 30 a) preparing a nucleic acid library starting from any suitable nucleic acid sequence which codes for a protein fragment of the sequence
- His-X<sup>1</sup>-His-X<sup>2</sup>-X<sup>3</sup>-X<sup>4</sup>-Cys-X<sup>5</sup>-X<sup>6</sup>-Cys,
- 35 where the histidine and cysteine residues of the sequence are conserved in the nucleic acid library,
- b) fusing the nucleic acids of the library to a reporter gene which makes it possible to detect the fusion protein encoded by the resulting nucleic acid via its binding to
- 40 the immobilized metal ions and
- c) selecting the nucleic acid sequences which display a reversible binding to the immobilized metal ions which is
- 45 at least 1.5 times stronger than the sequence in the natural *Helicobacter pilori* [sic] ATPase-439.

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16. A process as claimed in claim 15, wherein the egf protein from *Aequoria victoria* is used as reporter gene.
- 5 17. A method for detecting proteins, which comprises detecting individual proteins which comprise a protein fragment as claimed in claim 1 in a protein mixture via antibodies which are directed against the protein fragment.
- 10 18. The use of a protein fragment as claimed in <sup>claim 1</sup> ~~any of claims 1 to 6~~ or of a nucleic acid fragment as ~~claimed in claim 8~~ for purifying proteins.

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